

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

Claim 1 (Currently Amended): An antigenic composition comprising ~~a selected~~

(a) a first component selected from the group consisting of

(i). at least one antigen from a pathogenic organism selected from the group consisting of a bacterium, a virus, a fungus or and a parasite, and

(ii). at least one polynucleotide sequence encoding at least one antigen from a pathogenic bacterium, virus, fungus or parasite, said antigen-encoding sequence being under the control of a regulatory sequence directing expression of said antigen in a vertebrate host cell; and

(b) a second component selected from the group consisting of

(i). an effective adjuvanting amount of a mutant cholera holotoxin, wherein the mutant holotoxin has reduced toxicity compared to a wild-type cholera holotoxin and has a substitution at amino acid position 29 of the A subunit of the cholera holotoxin, wherein the glutamic acid residue is replaced by an amino acid other than aspartic acid, and wherein said mutant holotoxin enhances the immune response in a vertebrate host to said antigen, and

(ii). a polynucleotide sequence encoding the mutant cholera holotoxin of (b) (i), said sequence being under the control of a regulatory sequence directing expression of said mutant holotoxin in a vertebrate host cell.

Claim 2 (Currently Amended): The antigenic composition of Claim 1 wherein the antigenic composition comprises more than one ~~antigen~~ first component of (a).

Claim 3 (Original): The antigenic composition of Claim 1 wherein the amino acid at position 29 is histidine.

Appl. No. 09/806,370
Amdt dated November 10, 2003
Reply to Office Action of July 8, 2003

Claim 4(Currently Amended): The antigenic composition of Claim 1 wherein the ~~selected-antigen~~ first component of (a) is selected from the group consisting of the *Haemophilus influenzae* P4 outer membrane protein, the *Haemophilus influenzae* P6 outer membrane protein, the *Haemophilus influenzae* adherence and penetration protein (Hap_s), the *Helicobacter pylori* urease protein, the *Neisseria meningitidis* Group B recombinant class 1 pilin (rpilin), the *Neisseria meningitidis* Group B class 1 outer membrane protein (PorA), the respiratory syncytial virus fusion protein, a rotavirus virus-like particle ~~or~~ and the herpes simplex virus (HSV) type 2 glycoprotein D (gD2).

Claim 5(Currently Amended): The antigenic composition of Claim 4 wherein the ~~selected-antigen~~ at least one first component of (a) is selected from the group consisting of the *Haemophilus influenzae* P4 outer membrane protein, the *Haemophilus influenzae* P6 outer membrane protein, the *Haemophilus influenzae* Hap_s protein, ~~or~~ and any combination thereof.

Claim 6(Currently Amended): The antigenic composition of Claim 4 wherein the ~~selected-antigen~~ first component of (a) is the *Helicobacter pylori* urease protein.

Claim 7(Currently Amended): The antigenic composition of Claim 4 wherein the ~~selected-antigen~~ at least one first component of (a) is selected from the group consisting of the *Neisseria meningitidis* rpilin, *Neisseria meningitidis* PorA protein ~~or~~ and any combination thereof.

Claim 8(Currently Amended): The antigenic composition of Claim 4 wherein the ~~selected-antigen~~ first component of (a) is the respiratory syncytial virus fusion protein.

Claim 9(Currently Amended): The antigenic composition of Claim 4 wherein the ~~selected-antigen~~ first component of (a) is a rotavirus virus-like particle.

Claim 10(Original): The antigenic composition of Claim 9 wherein the virus-like particle is a rotavirus 2/6-virus-like particle.

Appl. No. 09/806,370
Amdt dated November 10, 2003
Reply to Office Action of July 8, 2003

Claim 11(Currently Amended): The antigenic composition of Claim 4 wherein the ~~selected antigen~~ first component of (a) is HSV gD2.

Claim 12(Currently Amended): The antigenic composition of Claim ~~11~~ 1, wherein the ~~antigenic composition is a~~ polynucleotide sequence of (a) vaccine comprising comprises plasmid DNA encoding HSV gD2.

Claim 13(Original): The antigenic composition of Claim 1 wherein the antigenic composition further comprises a diluent or carrier.

Claim 14(Original): The antigenic composition of Claim 1 which further comprises a second adjuvant in addition to the mutant cholera holotoxin.

Claim 15(Currently Amended): The antigenic composition of Claim 1, wherein at least one additional mutation is made to the A subunit of the mutant cholera holotoxin at a position other than amino acid 29, wherein said mutant holotoxin with said additional mutation enhances the immune response in a vertebrate host to said antigen.

Claim 16(Currently Amended): The antigenic composition of Claim 15 wherein the at least one additional mutation is made as a substitution for an amino acid of cholera holotoxin selected from the group consisting of the arginine at amino acid 7, the aspartic acid at position 9, the arginine at position 11, the histidine at position 44, the valine at position 53, the arginine at position 54, the serine at position 61, the serine at position 63, the histidine at position 70, the valine at position 97, the tyrosine at position 104, the praline at position 106, the histidine at position 1076, the serine at position 109, the glutamic acid at position 100, the glutamic acid at position 112, the serine at position 114, the tryptophan at position 127, the arginine at position 146 and the arginine at position 192.

Claim 17(Currently Amended): A method for increasing the ability of an antigenic composition containing ~~a selected~~ at least one antigen from a pathogenic organism selected from the group consisting of a bacterium, a virus, a fungus or a parasite to elicit the immune

Appl. No. 09/806,370
Amdt dated November 10, 2003
Reply to Office Action of July 8, 2003

response of a vertebrate host, which comprises administering to said host an antigenic composition of Claim 1.

Claims 18-23 (Canceled)

Claim 24 (Currently Amended): A plasmid containing an isolated and purified DNA sequence comprising a DNA sequence which ~~encode an immunogenic~~ encodes a mutant cholera holotoxin, which serves as an adjuvant, having a substitution at amino acid position 29 of the A subunit of the wild-type cholera holotoxin, wherein the glutamic acid residue is replaced by an amino acid other than aspartic acid, and wherein the DNA sequence is operatively linked to an arabinose inducible promoter.

Claim 25(Original): A host cell transformed, transduced or transfected with the plasmid of Claim 24.

Claim 26(Currently Amended): A method of producing ~~an immunogenic~~ a mutant cholera holotoxin, which serves as an adjuvant, ~~wherein the cholera holotoxin has reduced toxicity compared to a wild-type cholera holotoxin and has substitution at position 29 of the A subunit of the cholera holotoxin, wherein the glutamic acid residue is replaced by an amino acid other than aspartic acid, and~~ which comprises the steps of:

- (a) transforming, transducing or transfecting a host cell with the plasmid of Claim 24; and
- (b) culturing the host cell under conditions which permit the expression of said ~~recombinant immunogenic detoxified protein~~ mutant cholera holotoxin by the host cell; and
- (c) recovering said expressed holotoxin.

Claim 27(Canceled).

Claim 28 (Currently Amended): The method of Claim 17 wherein the antigenic composition comprises more than one ~~antigen~~ first component of (a).

Appl. No. 09/806,370
Amdt dated November 10, 2003
Reply to Office Action of July 8, 2003

Claim 29(Original): The method of Claim 17 wherein the amino acid at position 29 is histidine.

Claim 30(Currently Amended): The method of Claim 17 wherein the ~~selected antigen~~ first component of (a) is selected from the group consisting of the *Haemophilus influenzae* P4 outer membrane protein, the *Haemophilus influenzae* P6 outer membrane protein, the *Haemophilus influenzae* Hap_s protein, the *Helicobacter pylori* urease protein, the *Neisseria meningitidis* rpilin, the *Neisseria meningitidis* PorA protein, the respiratory syncytial virus fusion protein, a rotavirus, virus-like particle ~~or~~ and HSV gD2.

Claim 31(Currently Amended): The method of Claim 30 wherein the ~~selected antigen~~ at least one first component of (a) is selected from the group consisting of the *Haemophilus influenzae* P4 outer membrane protein, the *Haemophilus influenzae* P6 outer membrane protein, the *Haemophilus influenzae* Hap_s protein, ~~or~~ and any combination thereof.

Claim 32(Currently Amended): The method of Claim 30 wherein the ~~selected antigen~~ first component of (a) is the *Helicobacter pylori* urease protein.

Claim 33(Currently Amended): The method of Claim 30 wherein the ~~selected antigen~~ at least one first component of (a) is selected from the group consisting of the *Neisseria meningitidis* rpilin, *Neisseria meningitidis* PorA protein ~~or~~ and any combination thereof.

Claim 34(Currently Amended): The method of Claim 30 wherein the ~~selected antigen~~ first component of (a) is the respiratory syncytial virus fusion protein.

Claim 35(Currently Amended): The method of Claim 30 wherein the ~~selected antigen~~ first component of (a) is a rotavirus virus-like particle.

Claim 36(Original): The method of Claim 35 wherein the virus-like particle is a rotavirus 2/6-virus-like particle.

Appl. No. 09/806,370
Amdt dated November 10, 2003
Reply to Office Action of July 8, 2003

Claim 37(Currently Amended): The method of Claim 30 wherein the ~~selected antigen~~
first component of (a) is HSV gD2.

Claim 38(Currently Amended): The method of Claim 37 wherein the ~~antigenic~~
~~composition is a~~ polynucleotide sequence of (a) vaccine comprising comprises plasmid DNA
encoding HSV gD2.

Claim 39(Original): The method of Claim 17 wherein the antigenic composition further
comprises a diluent or carrier.

Claim 40(Original): The method of Claim 17 wherein the antigenic composition further
comprises a second adjuvant in addition to the mutant cholera holotoxin.

Claim 41(Currently Amended): The method of Claim 17 wherein at least one additional
mutation is made to the A subunit of the mutant cholera holotoxin at a position other than
amino acid 29, wherein said mutant holotoxin with said additional mutation enhances the
immune response in a vertebrate host to said antigen.

Claim 42(Currently Amended): The method of Claim 41 wherein the at least one additional
mutation is made as a substitution for an amino acid of cholera holotoxin selected from the
group consisting of the arginine at amino acid 7, the aspartic acid at position 9, the arginine at
position 11, the histidine at position 44, the valine at position 53, the arginine at position 54,
the serine at position 61, the serine at position 63, the histidine at position 70, the valine at
position 97, the tyrosine at position 104, the proline at position 106, the histidine at position
107, the serine at position 109, the glutamic acid at position 100, the glutamic acid at
position 112, the serine at position 114, the tryptophan at position 127, the arginine at
position 146 and the arginine at position 192.

Claim 43(New): A method of preparing an antigenic composition comprising combining

- (a) a first component selected from the group consisting of
 - (i) at least one antigen from a pathogenic organism selected from the group consisting of a bacterium, a virus, a fungus or and a parasite, and
 - (ii) at least one polynucleotide sequence encoding at least one antigen from a pathogenic bacterium, virus, fungus or parasite, said antigen-encoding sequence being under the control of a regulatory sequence directing expression of said antigen in a vertebrate host cell; and
- (b) a second component selected from the group consisting of
 - (i) an effective adjuvanting amount of a mutant cholera holotoxin, wherein the mutant holotoxin has reduced toxicity compared to a wild-type cholera holotoxin and has a substitution at amino acid position 29 of the A subunit of the cholera holotoxin, wherein the glutamic acid residue is replaced by an amino acid other than aspartic acid, and wherein said mutant holotoxin enhances the immune response in a vertebrate host to said antigen, and
 - (ii) a polynucleotide sequence encoding the mutant cholera holotoxin of (b) (i), said sequence being under the control of a regulatory sequence directing expression of said mutant holotoxin in a vertebrate host cell.